Functional Modules Distinguish Human Induced Pluripotent Stem Cells from Embryonic Stem Cells.

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Public Summary:
We describe in this study that human induced pluripotent stem cells (iPSCs) and embryonic stem cells (ESCs) exhibit different patterns of gene expression network. Using a method gene co-expression analysis, we found that iPSCs and ESCs differentially express 17 sets of genes involved in gene transcription, metabolism, development, and immune response. We further demonstrated that the overall levels of gene expression in these different modules are inversely correlated with a DNA modification called DNA methylation that normally leads to gene silencing. We conclude that human iPSCs and ESCs have differences in gene expression and DNA modification, and these differences could be used for distinguishing these two cell types.

Scientific Abstract:
It has been debated whether human induced pluripotent stem cells (iPSCs) and embryonic stem cells (ESCs) express distinctive transcriptomes. By using the method of weighted gene co-expression network analysis, we showed here that iPSCs exhibit altered functional modules compared with ESCs. Notably, iPSCs and ESCs differentially express 17 modules that primarily function in transcription, metabolism, development, and immune response. These module activations (up- and downregulation) are highly conserved in a variety of iPSCs, and genes in each module are coherently co-expressed. Furthermore, the activation levels of these modular genes can be used as quantitative variables to discriminate iPSCs and ESCs with high accuracy (96%). Thus, differential activations of these functional modules are the conserved features distinguishing iPSCs from ESCs. Strikingly, the overall activation level of these modules is inversely correlated with the DNA methylation level, suggesting that DNA methylation may be one mechanism regulating the module differences. Overall, we conclude that human iPSCs and ESCs exhibit distinct gene expression networks, which are likely associated with different epigenetic reprogramming events during the derivation of iPSCs and ESCs.